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Page 2 of 8

Preliminary Amendment

Applicant(s): GANAPATHY et al.
Serial No. 10/718,359
Filed: November 20, 2003

For: NaCT AS A TARGET FOR LIFESPAN EXPANSION AND WEIGHT REDUCTION

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1-11. (Cancel)

12. (Currently amended) An isolated polypeptide, wherein the polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the polynucleotide encodes a polypeptide demonstrating is capable of Na^+ -dependent transmembrane transport of citrate.

13. (Currently amended) The isolated polynucleotide polypeptide of claim 12, wherein the polynucleotide polypeptide comprises SEQ ID NO:6 [[5]].

14-19. (Cancel)

20. (Currently Amended) An isolated polynucleotide encoding a polypeptide comprising an amino acid sequence having at least 75 [[35]]% sequence identity to SEQ ID NO:6, wherein the polynucleotide encodes a polypeptide demonstrating is capable of Na^+ -dependent transmembrane transport of citrate.

21. (Original) The isolated polynucleotide of claim 20, wherein the encoded Na^+ -dependent transmembrane transport of citrate is modulated by Li^+ .

22-26. (Cancel)

27. (Currently Amended) The isolated polynucleotide polypeptide of claim 20, wherein the encoded polypeptide demonstrating capable of Na^+ -dependent transmembrane transport of citrate demonstrates a requirement for requires multiple Na^+ ions for transport coupling.

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Page 3 of 8

28. (Currently Amended) The isolated polynucleotide polypeptide of claim 20, wherein the transmembrane transport of citrate is electrogenic.

29-35. (Cancel)

36. (Currently amended) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 80 [[35]]% identity with to SEQ ID NO:6 [[2]], wherein the polypeptide is a transmembrane transporter of citrate.

37-44. (Cancel)

45. (Currently amended) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least [[35%]] 85% sequence identity to SEQ ID NO:6, wherein the polypeptide demonstrates Na^+ -dependent transmembrane transport of citrate.

46. (Cancel)

47. (Currently Amendment) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 90 [[75]]% sequence identity to SEQ ID NO:6, wherein the polypeptide demonstrates Na^+ -dependent transmembrane transport of citrate.

48. (Cancel)

49. (Currently Amended) The [[An]] isolated polypeptide, of claim 20, the polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:6, wherein the polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:1 under stringent hybridization conditions and wherein the polypeptide demonstrates transmembrane transport of citrate.

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50. (Currently Amended) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 99 [[35]]% sequence identity to SEQ ID NO:6 [[8]], wherein the polypeptide demonstrates Na^+ -dependent transmembrane transport citrate.

51-56. (Cancel)

57. (Currently Amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 having at least 35% identity with SEQ ID NO:2 with an agent;

measuring citrate transport into the host cell in the presence of agent;
and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

58. (Currently Amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 having at least 35% sequence identity to SEQ ID NO:8, wherein the transmembrane citrate transporter polypeptide demonstrates Na^+ -dependent transmembrane transport of citrate with an agent;

measuring citrate transport into the host cell in the presence of agent;
and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

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For: NaCT AS A TARGET FOR LIFESPAN EXPANSION AND WEIGHT REDUCTION

Page 5 of 8

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

59. (Currently Amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 having at least 35% sequence identity to SEQ ID NO.6, wherein the transmembrane citrate transporter polypeptide demonstrates Na⁺-dependent transmembrane transport of citrate and with an agent wherein the encoded Na⁺-dependent transmembrane transport of citrate is stimulated by Li⁺;

measuring citrate transport into the host cell in the presence of agent; and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

60-75. (Cancel)

76. (Currently Amended) A method of identifying an agent that modifies Na⁺-dependent transmembrane citrate transporter activity comprising:

contacting a host cell expressing a Na⁺-dependent transmembrane citrate transporter selected from the group consisting of SEQ ID NO.4, SEQ ID NO.6, SEQ ID NO.8, SEQ ID NO.10, and SEQ ID NO.12 of claim 12 with an agent;

measuring the citrate-induced inward electrical current into the host cell in the presence of agent; and

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For: NaCT AS A TARGET FOR LIFESPAN EXPANSION AND WEIGHT REDUCTION

Page 6 of 8

comparing the citrate-induced inward electrical current into the host cell in the presence of the agent to the citrate-induced inward electrical current into the host cell in the absence of the agent;

wherein a decrease in the inward electrical current into the host cell in the presence of the agent indicates the agent is a blocker of Na^+ -dependent transmembrane citrate transporter activity;

wherein an increase in the inward electrical current into the host cell in the presence of the agent indicates the agent is a stimulator of Na^+ -dependent transmembrane citrate transporter activity.

77. (Currently Amended) A method of identifying an agent that serves as a substrate of a Na^+ -dependent transmembrane citrate transporter comprising:

contacting a host cell expressing a Na^+ -dependent transmembrane citrate transporter selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, and SEQ ID NO:12 of claim 12 with an agent; and

determining the entry of the agent into the cell via the Na^+ -dependent transmembrane citrate transporter in the presence of agent;

wherein entry of the agent via the Na^+ -dependent transmembrane citrate transporter indicates the agent is a substrate of a Na^+ -dependent transmembrane citrate transporter.

78. (New) A recombinant polypeptide, wherein the recombinant polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the recombinant polypeptide is capable of Na^+ -dependent transmembrane transport of citrate.

79. (New) The recombinant polypeptide of claim 78, wherein the recombinant polypeptide comprises SEQ ID NO:6.

Preliminary Amendment

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Serial No. 10/718,359

Filed: November 20, 2003

For: NaCT AS A TARGET FOR LIFESPAN EXPANSION AND WEIGHT REDUCTION

Page 7 of 8

80. (New) A recombinant polypeptide comprising an amino acid sequence having at least 75% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na^+ -dependent transmembrane transport of citrate.

81. (New) The recombinant polypeptide of claim 80, wherein the encoded Na^+ -dependent transmembrane transport of citrate is modulated by Li^+ .

82. (New) A recombinant polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na^+ -dependent transmembrane transport of citrate.

83. (New) The recombinant polypeptide of claim 82, wherein the Na^+ -dependent transmembrane transport of citrate is modulated by Li^+ .